3. Other salts of *n*-alkyl ethers of β-*n*-alkylcholines have been formed from the bromides.

4. It has been shown that tetramethylammonium bromide and dimethyl-β-alkoxy-*n*-alkylamine are also formed in varying amounts in the reaction between trimethylamine and β-alkoxy-*n*-alkyl bromides.

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Some Halogenated Pinacolones

BY G. ALBERT HILL AND EDWARD L. KROPA

This investigation was undertaken to discover attractive methods for the preparation of the monohalogenated pinacolones. It was subsequently decided to complete the series of substances of the types

$$(CH)_3C—CO—CH_2X \quad (CH_3)_3C—CO—CHX_2 \quad (CH_3)_3C—CO—CX_3$$

as far as possible. Hitherto the dichloro-, and the mono-, di- and tribromo- derivatives have been reported.

A distinct relation between the speeds of the reactions and the generally recognized enolizing powers of the solvents employed indicated that the mechanism of the halogenation process, with free halogens, proceeds through enolic tautomers.

It is a pleasure to acknowledge the great benefit accruing to us from certain preliminary experiments carried out in this Laboratory by G. M. Bramann, by F. W. Lane and by V. S. Salvin. The material aid from the Atwater Fund has been of the greatest assistance.

Experimental

Pinacol hydrate was prepared by a modification of the Adams method.[1]

A four-foot condenser, with an inner tube 20 mm., and an outer jacket 55 mm., in diameter was used. All chemicals were scrupulously dried, and the reaction was allowed to run vigorously. The precipitation of the pinacol hydrate was carried out by ice, rather than by water, and gave fine, needle-like, friable crystals, which were readily purified by centrifuging and by centrifugal washing. By these means 45% yields of dry, pure white crystals were consistently obtained. This is significant since it has been shown[2] that pinacol hydrate air-dried for twenty-four hours still contains 4.9% of uncombined water. Earlier, unreported observations made in this Laboratory showed that apparently dry pinacol hydrate, which had not been centrifuged, lost considerable water when centrifuged.

Pinacolone was obtained from pinacol hydrate by treatment with sulfuric acid[3] and

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(1) R. and E. W. Adams, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1925, Vol. V, p. 87.

(2) King and Stewart, *Proc. Trans. Nova Scotian Inst. Sci.*, **17**, 262 (1930).

(3) Hill and Flosdorf, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1925, Vol. V, p. 91.

with yields consistently better than 72%. The melting point of pinacolone was found to be −49.8°, 2.7° higher than then reported.[4]

Monochloropinacolone.—Forty grams of pinacolone in 150 cc. of carbon tetrachloride was placed in a quartz flask provided with an internal condenser. The flask contents were kept at 20°, though the flask was near a strong ultraviolet light source. Chlorine was introduced until a 13-g. increase in weight took place. This required about an hour. The solution was washed immediately with ice water and dried with anhydrous sodium sulfate. The solvent was removed at a low pressure and the residue fractionally distilled; 12.4 g. of material, a 23% yield, boiled at 60.5° at 7 mm. It remained colorless for more than three months. All the halogenated pinacolones, with the exception of the dichloro compound, turn yellow, orange and finally black. The setting point, using a pentane thermometer, was found to be −12.6°.

Anal. Stepanoff method. Sample, 0.1736, 0.1744 g.; cc. of 0.10000 *N* $AgNO_3$, 160.86, 150.00; cc. of 0.09877 *N* NaSCN, 31.36, 20.26. Calcd. for $C_6H_{11}OCl$: Cl, 26.35. Found: Cl, 26.54, 26.43.

This highly lachrymatory ketone is difficult to prepare because of the extreme readiness with which the dichloro compound forms. Chlorination in cold chloroform and in carbon disulfide, in the absence and in the presence of water, was undertaken. Catalysts, such as iron and iodine, were experimented with, and buffering materials, such as marble and sodium carbonate, were employed. Electrolytic methods with platinum electrodes and with a platinum cathode and a carbon anode were also investigated. The method given above is the most satisfactory.

Dichloropinacolone was prepared by a modification of Fittig's method.[5] Forty grams of pinacolone was mixed with 10 cc. of water and the system cooled to 0° as chlorine was passed in. Dichloropinacolone crystallized spontaneously. After recrystallization from petroleum ether this substance melted at 51°. The yield was 35.2 g., 52%.

Trichloropinacolone.—This ketone was prepared by mixing pinacolone with ten times its volume of water, adding mercuric oxide in excess of that required to react with the three molecules of hydrochloric acid which would result, and passing in chlorine, with stirring. In the cold the operation was run for thirty hours, on a steam-bath for sixteen hours. The product was obtained by vacuum steam distillation, extraction with ether, drying with sodium sulfate and subsequent vacuum distillation. It is a colorless liquid, boiling at 101–102° at 8 mm., and gradually became dark on standing. No percentage yields were determined.

Anal. Stepanoff method. Sample, 0.2146 g.; cc. of 0.10000 *N* $AgNO_3$, 32.71; cc. of 0.99607 *N* NaSCN, 1.06. Calcd. for $C_6H_9OCl_3$: Cl, 52.31. Found: Cl, 52.29. *Anal.* Parr sulfur bomb.[6] Subs., 0.3881; cc. of 0.09982 *N* $AgNO_3$, 60.05; cc. of 0.10005 *N* NH_4SCN, 28.00. Calcd.: Cl, 52.31. Found: Cl, 52.27.

Attempts to prepare this compound by chlorination in sodium hydroxide were unsuccessful. When bleaching powder was used the desired compound was formed, but decomposed immediately.

Monobromopinacolone.[7]—One gram of aluminum amalgam and 500 cc. of dry ether were placed in a liter flask equipped with a stirrer, thermometer and a dropping funnel; 40 g. of pinacolone was added and after the system had been brought to 0°, 63 g. of bromine was added by drops, while the reactants were maintained at 0°. This process required half an hour. The solution was then permitted to come to room temperature. After three and one-half to four hours, during which

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[4] "International Critical Tables," Vol. I, p. 322, No. 1630.

[5] Fittig, *Ann.*, **114**, 60 (1860).

[6] Analysis by F. W. Lane.

[7] Widman and Wahlberg, *Ber.*, **44**, 2066 (1911).

stirring was continued, marked decolorization of the deep red liquid to a pale yellow took place almost instantaneously. The solution was transferred at once to a separatory funnel and freed from acid by washing with 250 cc. of ice cold water. The aqueous layer was separated, and extracted successively with four 50-cc. portions of ether. The combined ether solutions were dried with anhydrous sodium sulfate, and the ether subsequently removed under diminished pressure. The residue was subjected to vacuum fractionation. A yellow oil of unknown composition distilled first; 49 g. of bromopinacolone, a 68.4% yield, was obtained, and boiled at 71.5–72° at 10 mm. If distillation were attempted at above 15 mm. pressure, decomposition invariably occurred. The halogenated ketone melted at −10.5°. Upon standing the colorless, exceedingly lachrymatory compound gradually turned yellow. Without stirring the yield was 3% less, while in the absence of the catalyst the maximum yield was 54%, and the reaction took much longer.[8] These directions are based on seventeen experimental runs introducing numerous variables, *e. g.*, solvent, catalyst, etc.

Action of Ultraviolet Light on Monobromopinacolone.—Twenty grams of freshly distilled monobromopinacolone was enclosed in a quartz flask which was kept within 15 cm. of an ultraviolet light source for six hours. The originally colorless solution became yellow and then orange. No free bromine was detected. Upon vacuum distillation most of the material was found to be unchanged monobromopinacolone, but 5 g. of dibromopinacolone, m. p. 70–71°, was obtained. No low-boiling yellow oil resulted; hence, the first runnings in the isolation of monobromopinacolone were probably not formed by the action of light, and are, presumably, caused by oxidation.

Dibromopinacolone[9] is the easiest of the bromopinacolones to prepare, but it is difficult to purify and isolate; 40 g. of pinacolone and 1 g. of aluminum amalgam in 500 cc. of dry ether were treated with 126 g. of bromine. After decolorization, the ether solution was washed and dried with anhydrous sodium sulfate. The ether was removed under low pressure and was replaced by petroleum ether, from which 87.2 g., a 78% yield, of dibromopinacolone crystallized. When centrifuged the white crystals of this halogenated ketone became pink, probably due to oxidation. At great loss, about 66%, a highly purified material can be prepared by sublimation. The residue is a black gummy mass. The pure crystals melt sharply at 76.5°. Dibromopinacolone boils at 96.5–97° at 12 mm.

Tribromopinacolone[10] was prepared by treating 130 g. of mercuric oxide, and 40 g. of pinacolone, in 250 cc. of water, with 192 g. of bromine in 250 cc. of carbon tetrachloride. The system was stirred and refluxed for ninety-six hours before complete decolorization took place. The mercuric bromide which formed collected at the liquid interface and was removed by filtration. After separating, the carbon tetrachloride layer was dried with anhydrous sodium sulfate. The solvent was removed at a low pressure and the residue fractionated in a vacuum. Tribromopinacolone distilled at 116–117° at 15.5 mm., as a yellow oil which crystallized on standing. In order to prepare the trihalo ketone free from the dibromo compound, it is necessary to use an excess of mercuric oxide and of bromine.

Monoiodopinacolone.—A modified Scholl and Mattaipolus method[11] was used to prepare this compound; 11.1 g. of potassium iodide in 8 cc. of water was added to 225 cc. of methyl alcohol containing 12 g. of monobromopinacolone and gave a homogeneous liquid system. The reaction vessel was kept in the dark, at room temperature, for twenty-four hours and then contained a precipitate, potassium bromide, in a deep orange solution. After filtration, the solvent was evaporated at a low pressure and the

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(8) This test was carried out by A. R. Taylor.

(9) Scholl and Weil, *Chem. Z.*, **23**, 189 (1899).

(10) Richard and Langlais, *Bull. soc. chim.*, [4] **7**, 465 (1910).

(11) Scholl and Mattaipolus, *Ber.*, **29**, 1557 (1896).

iodo ketone purified by a vacuum steam distillation at room temperature. Monoiodopinacolone, obtained as a salmon colored oily liquid, is denser than water. Taken up in petroleum ether, it imparted a violet color to the solution, presumably as a result of incipient decomposition.

A sample of the iodinated ketone was divided into four equal portions which were dissolved in equal volumes of methyl alcohol. Some of these tubes were kept in the dark, others in the light. After twenty-four hours the tube contents showed marked increase in color depth. Those kept in the light were affected to a greater extent. In each tube the color was deepest at the top. No appreciable evaporation had occurred; hence, light and especially air, *i. e.*, oxygen, cause the compound to decompose.

Diiodopinacolone.—Attempts to isolate diiodopinacolone were uniformly unsuccessful. When dibromopinacolone was mixed with an aqueous solution of potassium iodide the mixture promptly became orange, indicating synthesis and immediate decomposition.

Conclusions

1. Mono-, di- and tri-chloro-, mono-, di- and tri-bromo-, and mono-iodo-pinacolones have been prepared.
2. The mono-, and tri-chloro-compounds and the mono-iodo ketone are new.
3. By an improved method monobromopinacolone has been produced in good yields. A new method has been devised for the preparation of dibromopinacolone. The tribromo compound has been prepared by a new, and direct, method.
4. Attempts to isolate pure mono- and pure di-iodopinacolone were not successful. These substances seem to be unusually sensitive to light and to air.

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A New Method for the Preparation of the Free Acids and the Abnormal Lactones of the Monobasic Sugar Acids

BY JOHN M. BRACKENBURY AND FRED W. UPSON

The general procedure for the preparation of hexonic acids and in certain cases the corresponding δ-lactones has been by precipitation of the metallic radical of the salts, generally the calcium salt, evaporation of the aqueous solution *in vacuo* from a water-bath heated to 40–50° and extraction of the product with some suitable solvent for recrystallization.

Kiliani[1] prepared the first crystalline hexonic acid and assigned to it the empirical formula ($C_6H_{12}O_7$). He believed this acid to be monomolecular galactonic acid. Later Nef[2] and Hedenburg[3] made a study of this substance and showed that in the crystalline state the acid has instead the

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[1] Kiliani, *Ber.*, **18**, 1551 (1885).

[2] Nef, *Ann.*, **403**, 277 (1914).

[3] Hedenburg, THIS JOURNAL, **37**, 364 (1915).